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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/162,648	09/29/1998	JOHN C. HISERODT		9087

7590 02/13/2004

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EXAMINER	
CHEN, SHIN LIN	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 02/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/162,648	HISERODT, JOHN C.	
	Examiner	Art Unit	
	Shin-Lin Chen	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,18-20 and 22-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *23-31* is/are allowed.

6)☐ Claim(s) *1-14, 18-20, 22 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment and the declaration by Dr. John Hiserodt filed 10-31-03 have been entered. Claim 1 has been amended. Claim 32 has been added. Claims 15-17 and 21 have been canceled. Claims 1-14, 18-20 and 22-32 are pending and under consideration.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Claims 1-10, 12-14, 19, 20 and 22 remain rejected and claim 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Granger (US Patent 5,837,233) in view of Hiserodt et al., 1998, WO 98/16238 and is repeated for the reasons set forth in the preceding Official action mailed 12-18-02 (Paper No. 25). Applicant's arguments filed 10-31-03 have been fully considered but they are not persuasive.

Claim 32 is a newly added claim and is directed to the method of claim 1, wherein the first and second cell populations are implanted at or around the site of the same tumor in the patient.

Applicant argues that there is no motivation to combine the Granger patent and WO 98/16238 and declaration by Dr. Hiserodt explains that the present application is an improvement of the Granger method and is different from in nature and practice from WO 98/16328. WO

98/16326 requires use of tumor antigen and the mixture of cells is administered at a site away from the primary tumor. Granger teaches administering alloactivated cells directly into the tumor bed without any added tumor antigen and a single administration of the implant is sufficient to elicit an immune response against tumor. Applicant further argues that it is beneficial to leave tumor in the patient so as to provide bystander antigen for the second administration of alloactivated cells (amendment, p. 8, 9). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 12-18-02 (Paper No. 25). Hiserodt (WO 98/16238) not only teaches administering alloactivated allogeneic lymphocytes and tumor antigen at a site distant from the tumor (example 4) but also teaches direct intratumoral implantation of allogeneic lymphocytes activated against patient alloantigens by mixed lymphocyte culture (no tumor antigen is added) and shows such direct intratumoral implantation of MLC-activated allogeneic lymphocytes in patients is feasible, safe and beneficial clinically (example 1). Hiserodt further teaches that additional doses of the alloactivated lymphocytes may be given, such as on a monthly or weekly basis, until the desired effect is achieved (e.g. page 27).

Granger teaches implanting the alloactivated lymphocytes to the proximity of a surgically debulked tumor or an inoperable tumor, i.e. the tumor has not been removed (column 3), and teaches "In accordance with conventional prudent formulating practices, a dosage near the lower end of the useful range may be employed initially and the dosage increased or decreased as indicated from the observed response, as in the routine procedure of the physician" (column 5-6). Granger also states "More generally, a therapeutic amount may vary with the potency of each batch of alloactivated donor cells; the amount required for the desired therapeutic or other effect,

the mode of administration, i.e. whether by direct implant into a tumor or body cavity or by peripheral administration" (column 5, lines 57-61).

Both Granger and WO 98/16238 teach implanting alloactivated lymphocytes directly into tumor to illicit immune response against tumor in a patient. Granger implies administration of multiple doses of the alloactivated lymphocytes for the treatment of tumor and WO 98/16238 teaches that additional doses of the alloactivated lymphocytes may be given, such as on a monthly or weekly basis, until the desired effect is achieved. Both Granger and WO 98/16238 teach using alloactivated lymphocytes to illicit immune response against tumor in a patient. Therefore, it would have been obvious for one of ordinary skill at the time of the invention to administer more than one alloactivated lymphocyte cell populations to a tumor in a patient in order to generate a therapeutic or immunologic response against tumor growth as taught by Granger and Hiserodt. Thus, claims 1-10, 12-14, 19, 20 and 22 remain rejected and claim 32 is rejected under 35 U.S.C. 103(a).

3. Claims 11 and 18 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Granger (US Patent 5,837,233) in view of Hiserodt et al., 1998, WO 98/16238 as applied to claims 1-10, 12-14, 16, 19, 20 and 22-31 above, and further in view of Haugland (1992) and Jung (1990) and is repeated for the reasons set forth in the preceding Official action mailed 12-18-02 (Paper No. 25). Applicant's arguments filed 10-31-03 have been fully considered but they are not persuasive.

Applicant reiterates arguments regarding the cited references Granger and WO 98/16238 as above (amendment, p. 10). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 12-18-02 (Paper No. 25) and the reasons set forth above.

Applicant request examiner's affidavit for the statement "it was common practice at the time of the invention to have multiple administration to ensure better results of a treatment" (amendment, p. 10-11). In regarding this request by applicant, it should be noted that such statement by examiner is well evidenced in the references, Granger and WO 98/16238, cited by examiner.

Conclusion

Claims 1-14, 18-20, 22 and 32 are rejected. Claims 23-31 are in condition for allowance.

4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (571) 272-0726. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.

Shin-Lin Chen, Ph.D.